UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,379	09/27/2004	Shogo Ishiuchi	Q83588	5052

65565 7590 11/21/2008

SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
11/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,379	ISHIUCHI, SHOGO	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-12,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *13-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/27/04 and 01/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of IDS filed on 09/27/04 and 01/10/05 is acknowledged.

Restriction/Election

Applicant's election without traverse of Group IV, claims 13-16 and the elected compound "7-acetyl-5-(4-aminophenyl)-8(R)-methyl-8,9-dihydro-7H-1,3-dioxolo [4,5-h] [2,3]benzodiazepine (Talampanel) in the reply filed on 08/01/08 is acknowledged.

Claims 1-12 and 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/01/08.

Claims **13-16** are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See, e.g., In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984). (Holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.')

Mere indistinct terms and phrase (such as administering a **therapeutically effective amount** of a **compound having an activity of inhibiting an a-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)** receptor to a patient with the disease. used herein), however, may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely functional terms. See Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886 (CAFC 2004) at 1892, stating:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice…. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

Conversely, a description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See Univ. of Calf. V. Eli Lilly, 43 USPQ 2d 1398, 1406

(Fed. Cir. 1997). This is analogous to enablement of a genus under Section 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. *If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus*. See MPEP 2163. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any *combination of such identifying characteristics that distinguish the claimed invention from other materials* and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Here, the specification does not provide a reasonably representative disclosure of useful [each and every compound that possibly exists in pharmaceutical art **having an activity of inhibiting an a-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA**] generally, a potentially huge genus inclusive of many different compounds having widely divergent structures and functions. Specifically, the specification discloses only a limited number of species at page [14], lines [19-25], and these are not viewed as being reasonably representative of the genus in its claimed scope because no readily

apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

Scope of Enablement

4. Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "7-acetyl-5-(4-aminophenyl)-8(R)-methyl-8,9-dihydro-7H-1,3-dioxolo [4,5-h] [2,3]benzodiazepine (Talampanel) in treating glioblastoma does not reasonably provide enablement for each and every compound claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

A method for treating glioblastoma comprising administering a therapeutically effective amount of a compound having an activity of inhibiting an a-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor to a patient with the disease.

The invention relates to method of treating glioblastoma comprising administering a therapeutically effective amount of a compound having an activity of inhibiting an a-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor to a

patient with the disease. The claims do not recite **specific amount** of compound or **specific compound** which inhibits AMPA receptor to a patient.

The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art.

2. The breadth of the claim

The scope of the claims does not commensurate with the scope of the disclosure. The claims are very broad and as recited encompass unlimited compound and indefinite effective amount.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for practicing the claimed invention in its “full scope”. No reasonably specific guidance is provided concerning useful therapeutic protocols for compounds other than "7-acetyl-5-(4-aminophenyl)-8(R)-methyl-8,9-dihydro-7H-1,3-dioxolo [4,5-h] [2,3]benzodiazepine (Talampanel) .The latter is corroborated by the working examples.

[The instant disclosure provides no evidence to suggest that this unique activity can be extended to any compound and thus does not meet the “how to use” prong of 35 USC 112, first paragraph with regard thereto.]

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used without undue experimentation as

inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the limitation effective amount however no effective amount have been listed in claims. In the absence of specific amount or specific range of amounts, the claim would read on any amount (high or low). As such the claim is indefinite.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

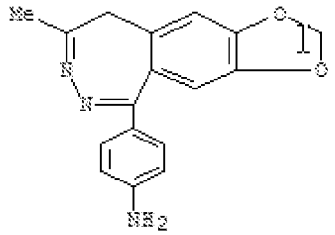
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Paulsen et al. (WO 03/000928) in view of Andrasi et al. (USP 5,639,751) or vice versa.

Paulsen et al. teach cancer cell cell-surface molecule and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods (title).

RN 102771-26-6 HCAPLUS
CN Benzenamine, 4-(8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepin-5-yl)-
(CA INDEX NAME)

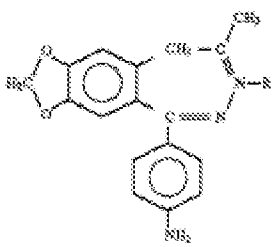


The reference differs from instant compound by acyl group.

Andrasi et al. teach the claimed compound and the use of such compound in treating various diseases of central nervous system. (Abstract). These compounds have been characterized as having a property of inhibiting AMPA receptors. (See column 3 as depicted below.

According to the invention, the compounds of the formula (I) are prepared by

a) acylating a compound of the formula (II)



with a C_{1-6}alkanoic acid optionally substituted by a methoxy, cyano, carboxyl or phenyl group or by one or more halogen(s); or with benzoic, cyclopropanecarboxylic or palmitic acid or with a reactive derivative thereof; and, if desired, reacting a new compound of the formula (I) thus obtained, wherein R^4 is a C_{1-6}alkanoyl group substituted by a halogen, with a C_{1-6}alkylamine, di(C_{1-6}alkyl)amine or pyrrolidine, to obtain compounds of the formula (I), wherein R^2, R^3 and the dotted lines are as defined above, R^4 is a C_{1-6}alkanoyl group optionally substituted by a methoxy, cyano, carboxyl, phenyl, C_{1-6}alkylamino, di(C_{1-6}alkyl) amino or pyrrolidino group or one or more halogen(s); or a benzoyl, cyclopropanecarbonyl or palmitoyl group; R and R^1 are absent and a double bond is present between the N(3) and C(4) atoms;

It would have been obvious to one of ordinary skill in the art at the time of invention to substitute **acyl group** and come to the claimed invention. One would have been motivated because the reference teaches equivalency of the compound as disclosed by Paulsen et al. with the claimed compound Talampanel. Andrasi also teaches that talampanel is AMPA receptor antagonist. Paulsen teaches similar compounds as discussed above in cancer treatment methods. (Instant specification describes pharmaceutical use of a compound having an antagonistic action against AMPA receptor as a therapeutic agent for glioblastoma.on page 1).

As such, it would have been obvious to one of ordinary skill in the art to utilize the compounds taught by Andrasi et. al. and Paulsen et al. in treating glioblastoma and arrive at the claimed invention with the reasonable expectation of success. One would have been motivated to do so with an expectation of treatment of glioblastoma since

Paulsen teaches that such compounds are useful in treating cancer and Andrasi teaches the compound to AMPA receptor antagonist.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/
Examiner, Art Unit 1612
/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612